

# Botryoid Embryonal Rhabdomyosarcoma of the Uterine Cervix in Nulliparous Woman: Fertility-Conscious Multimodal Management of IRSG Group III Disease

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## Abstract

**Background:** Botryoid embryonal rhabdomyosarcoma (ERMS) of the uterine cervix is an uncommon mesenchymal malignancy in reproductive-aged women. The botryoid variant typically demonstrates polypoid morphology and favorable chemosensitivity, yet prognosis depends critically on tumor burden and completeness of local control. Adult cervical ERMS is rare and underrepresented in prospective trials, posing unique diagnostic and therapeutic dilemmas—especially when fertility preservation is desired. **Case presentation:** A 28-year-old nulliparous woman (P0000) presented with intermittent postcoital bleeding for ~12 months. Speculum examination revealed a friable, hump-shaped polypoid cervical mass that bled on contact. Pelvic MRI showed a large cervical tumor measuring 11.3 × 9.1 × 12.9 cm confined to the cervix without radiologic distant metastasis. Incisional biopsy demonstrated small round to spindle tumor cells with a subepithelial cambium layer; immunohistochemistry was positive for desmin, myogenin, and MyoD1—confirming botryoid ERMS. Because no complete surgical resection was performed and gross tumor remained, the case was classed as IRSG Group III. Given the large tumor burden and the patient's strong fertility desire, a fertility-conscious strategy was adopted: neoadjuvant systemic chemotherapy with six cycles of vincristine, actinomycin-D, and cyclophosphamide (VAC), with monthly clinical follow-up and interval MRI for response assessment. **Conclusion:** This case underscores (1) the need for high clinical suspicion and prompt tissue diagnosis for persistent abnormal bleeding, (2) the prognostic importance of tumor size and IRSG grouping in adult cervical ERMS, and (3) the pragmatic role of neoadjuvant VAC to downstage bulky Group III disease in patients seeking fertility preservation.

**Keywords:** embryonal rhabdomyosarcoma; botryoid; cervix cancer; VAC chemotherapy

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## Introduction

Rhabdomyosarcoma (RMS) is a malignant neoplasm of skeletal muscle lineage that primarily affects children and adolescents; adult presentations are rare and often demonstrate distinct clinical behavior and outcomes.<sup>1,2</sup> Within the female genital tract, embryonal rhabdomyosarcoma (ERMS) predominates, and the botryoid variant characteristically produces exophytic, polypoid masses with a subepithelial cambium layer on histology.<sup>3</sup> Although embryonal histology is associated with relatively favorable biology (frequently fusion-negative and chemosensitive), prognosis is not determined by histology alone: tumor size, clinical group (extent of residual disease after initial procedure), nodal/metastatic status, and primary site are major determinants of relapse risk and survival.<sup>4,5</sup>

Contemporary therapeutic paradigms for RMS are based mainly on Intergroup Rhabdomyosarcoma Study Group (IRSG) risk stratification and include combinations of surgery, systemic chemotherapy (typically vincristine, actinomycin-D, cyclophosphamide — VAC), and radiotherapy as indicated.<sup>5,6</sup> Adult cervical ERMS is infrequent and therefore underrepresented in prospective trials; management is commonly extrapolated from pediatric protocols but must be individualized—

particularly regarding organ preservation and fertility considerations.<sup>6,7</sup> We present a CARE-compliant case of bulky botryoid ERMS of the cervix (IRSG Group III) managed with a fertility-conscious neoadjuvant VAC strategy, and we integrate contemporary survival and risk-classification data to contextualize prognosis and therapeutic decisions.

## Patient Information

A 28-year-old woman, nulliparous (G0P0), was referred for evaluation of persistent postcoital bleeding for approximately 12 months. She reported progressive increase in bleeding over the previous 3 months. She denied pelvic pain, systemic symptoms, or prior gynecologic procedures. No significant past medical or family history of malignancy was reported. The patient expressed a strong desire for future fertility and preference for conservative treatment if oncologically safe.

## Clinical Findings

Speculum examination identified a fragile, hump-shaped polypoid mass arising from the cervix and obscuring the portio-upper vaginal boundary; the tumor bled on contact. Bimanual palpation revealed cervical

enlargement; there was no frank parametrial fixation on clinical exam and no palpable inguinal nodes.



Figure 1. Inspection

### Timeline

Month -12: Onset intermittent postcoital bleeding.

Month -1: Progressive bleeding → referral and speculum exam.

Day 0: Pelvic MRI and incisional cervical biopsy.

Day 7: Histopathology + IHC confirm botryoid ERMS.

Day 21: Multidisciplinary tumor board; decision for neoadjuvant VAC.

Weeks 4-24: Six cycles VAC, monthly clinical review; interval MRI planned after cycle 3 and cycle 6.

Ongoing: Monthly follow-up and imaging; plan for surgical reassessment pending response.

### Diagnostic Assessment

Imaging: Pelvic MRI revealed a predominantly solid cervical mass measuring  $11.3 \times 9.1 \times 12.9$  cm with heterogeneous signal intensity, localized to the cervix without radiologic evidence of pelvic nodal enlargement or distant metastasis. MRI findings guided surgical planning and baseline tumor burden quantification.

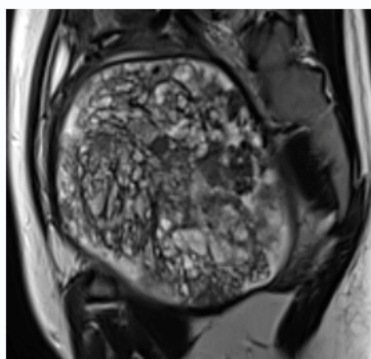


Figure 2. Magnetic Resonance Imaging

Abdominal USG results refers to malignant cervical mass measuring +/- 10.3 x 10.7 x 10.8 cm with the details and extension mentioned above accompanied by endometrial thickening, there was no visible metastasis process in the liver or enlargement of the para-aortic lymph nodes

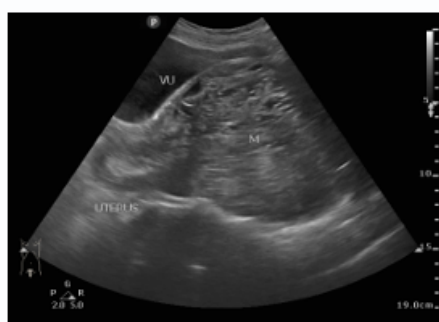


Figure 3. Ultrasonography

**Histopathology & Immunohistochemistry:** Incisional biopsy demonstrated small round to spindled tumor cells embedded in myxoid stroma with a prominent subepithelial cambium layer—morphology consistent with botryoid ERMS. Immunohistochemical staining was diffusely positive for desmin, myogenin, and MyoD1, confirming skeletal muscle differentiation and excluding morphologic mimics (e.g., lymphoma, poorly differentiated carcinoma, small-round-blue-cell tumors).<sup>7</sup>

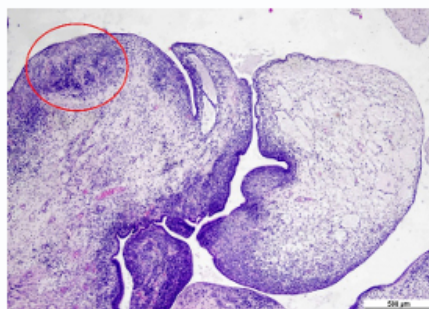


Figure 4. Cervical Biopsy

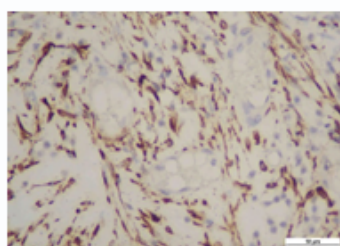


Figure 5. IHC Desmin

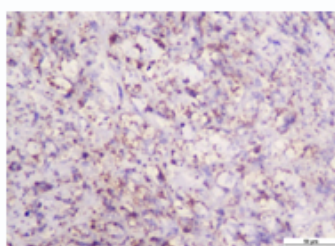


Figure 6. Myogenin

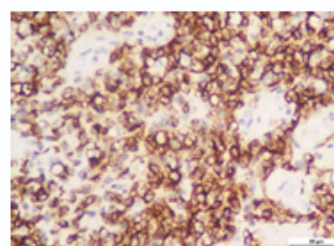


Figure 7. Smooth Muscle Actin

**IRSG Clinical Group & Risk Classification:** Because no complete oncologic resection was performed and gross residual tumor remained, the patient was categorized as IRSG Group III. Combining embryonal histology (favorable) with a large primary tumor (>10 cm) and Group III clinical status places the patient in an intermediate-risk bracket within contemporary COG/IRSG-derived stratification, with a correspondingly increased risk of local relapse compared with Groups I–II.<sup>4,5,8</sup>

### Therapeutic Intervention

Management was discussed and agreed upon at a multidisciplinary tumor board (gynecologic oncology, medical oncology, radiology, pathology, reproductive endocrinology). Given the bulky tumor, absence of metastasis, and the patient's fertility preference, a fertility-conscious neoadjuvant approach was chosen:

- **Systemic chemotherapy:** VAC regimen — vincristine (weekly or per protocol bolus), actinomycin-D, cyclophosphamide (doses per institutional pediatric-derived protocols with adult dose adjustments). The patient received six cycles of VAC over ~18 weeks with supportive care and growth factor support as indicated. VAC remains the backbone regimen for embryonal RMS and is the standard systemic modality to achieve cytoreduction in Group III disease.<sup>5,9</sup>
- **Surgery:** Deferred initially to enable tumor downsizing. Surgical options discussed contingent on response included fertility-sparing procedures (local wide excision or radical trachelectomy) vs

more radical hysterectomy if downstaging was insufficient.

- **Radiotherapy:** Reserved for persistent gross residual disease after chemotherapy and surgical assessment, in line with IRSG/COG guidance for local control in Group III settings.<sup>5</sup>
- **Fertility preservation measures:** The patient received counseling from reproductive endocrinology. Options discussed included oocyte or embryo cryopreservation prior to gonadotoxic therapy when feasible, and future assisted reproductive technologies (ART). Ovarian protection strategies (e.g., gonadotropin-releasing hormone analogues) and ovarian transposition would be considered only if pelvic radiotherapy becomes necessary.<sup>10,11</sup>

### Follow-Up and Outcomes

The patient was evaluated monthly, with clinical exam and hematologic monitoring during chemotherapy. Interval MRI was planned at mid-treatment (after cycle 3) and at completion (after cycle 6) to assess volumetric response (RECIST or volumetric percentage reduction to be reported). Toxicities were recorded using CTCAE v5.0; treatment was overall well tolerated with expected hematologic suppression manageable with supportive measures. Surgical reassessment will follow cycle-6 imaging to determine the feasibility of fertility-sparing resection.

### Discussion

#### Diagnostic Considerations and Differential

Botryoid ERMS of the cervix may masquerade as benign cervical polyps or other exophytic lesions, delaying diagnosis.<sup>1,3</sup> Persistent abnormal vaginal bleeding—especially postcoital bleeding that is prolonged—should prompt imaging and tissue diagnosis. MRI provides excellent soft-tissue delineation for local staging and surgical planning, while IHC markers (myogenin, MyoD1, desmin) are essential for diagnostic confirmation and to distinguish ERMS from other small round cell neoplasms and poorly differentiated carcinomas.<sup>7,10</sup>

### Risk Stratification and Prognostic Data

IRSG/COG risk frameworks integrate histology, tumor site, size, nodal/metastatic status, and clinical group to categorize patients into low, intermediate, and high risk—guiding therapy intensity.<sup>4,5,8</sup> Key prognostic drivers are:

- Histology: Embryonal (botryoid) histology generally confers better chemotherapy responsiveness and prognosis than alveolar (often FOXO1-fusion positive) subtypes.<sup>2,4</sup>
- Tumor size: Tumors >5 cm are associated with significantly worse event-free survival and overall survival across cooperative group analyses.<sup>4,8</sup>
- Clinical group: Group III (gross residual disease) carries higher local failure rates than Groups I–II and often requires combined modality therapy.<sup>5</sup>

Published survival figures for adult cervical ERMS are heterogeneous due to small series and case reports. Aggregated data suggest 5-year overall survival (OS) for localized embryonal RMS ranges approximately 65–75% in pediatric cohorts, whereas adult series report wider ranges (≈50–78%) influenced by site, stage, and treatment completeness.<sup>2,5,12</sup> Specifically, non-metastatic Group III embryonal RMS typically achieves 5-year OS in the ballpark of 55–75% with multimodal therapy; metastatic (Group IV) disease has substantially worse outcomes.<sup>4,5</sup> Botryoid histology often portends better local control, but bulky tumor size and incomplete resection (as in this case) attenuate this advantage.

Application to our case: Embryonal (botryoid) histology and non-metastatic status are favorable; conversely, tumor maximal diameter >10 cm and Group III status are adverse—together placing the patient within an intermediate-risk category. Therefore, the chosen neoadjuvant VAC strategy is consistent with evidence-based practice to achieve cytoreduction, improve resectability, and preserve fertility options when feasible.<sup>5,9,13</sup>

### Role of VAC and Systemic Therapy in Group III Disease

VAC (vincristine, actinomycin-D, cyclophosphamide) remains the cornerstone systemic therapy for embryonal RMS. Neoadjuvant VAC can effect substantial tumor shrinkage in embryonal histology, enabling fertility-preserving resections in selected cases.<sup>5,9</sup> Adult RMS series report variable chemosensitivity relative to

pediatric cohorts; nonetheless, VAC is accepted as first-line systemic therapy for non-metastatic embryonal variants in adults when extrapolating pediatric evidence.<sup>5</sup> Response assessment via MRI (RECIST or volumetric analysis) at defined intervals (after 2–3 cycles and at completion) is recommended to guide local control strategies.<sup>13</sup>

### Fertility Preservation Considerations

Fertility preservation is a central concern in young women with cervical malignancy. Options include oocyte/embryo cryopreservation prior to gonadotoxic chemotherapy, ovarian suppression protocols, ovarian transposition if pelvic radiotherapy is planned, and fertility-sparing surgery when oncologically appropriate.<sup>10,11</sup> For RMS specifically, case reports demonstrate feasibility of uterine-sparing approaches after significant neoadjuvant response, but robust prospective data are lacking.<sup>6,12</sup> Multidisciplinary counseling and early referral to reproductive specialists are essential.

### Limitations and Evidence Gaps

Adult cervical ERMS data are limited to case reports and small series, resulting in imprecise survival estimates and absence of adult-specific randomized data. Differences in adult tumor biology and tolerance to pediatric-based regimens underscore the need for adult-focused registries and trial inclusion. Reporting standardized outcomes—RECIST/volumetric response, CTCAE toxicity, fertility outcomes, and long-term oncologic follow-up—will meaningfully augment the evidence base.

### Conclusion

Botryoid ERMS of the cervix in adults is rare but potentially curable when managed with a multidisciplinary, risk-adapted approach. Tumor size and IRSG clinical grouping are pivotal prognostic factors: bulky Group III disease warrants systemic neoadjuvant therapy (VAC) to maximize the chance of conservative local control and fertility preservation. Comprehensive adult case reports with standardized response metrics and reproductive outcomes are urgently needed to refine adult-specific management algorithms.

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